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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/936,377	02/26/2002	Catherine Defrenne	BM45379	4141

25308 7590 01/16/2004

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EXAMINER	
BASKAR, PADMAVATHI	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 01/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/936,377	DEFRENNE ET AL.	
	Examiner	Art Unit	
	Padmavathi v Baskar	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10/20/03*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25,27,29,31,32,35,40,41,43 and 47-51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25,27,29,31,32,35,40,41,43 and 47-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *9/22/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Applicant's response to restriction filed on 10/20/03 is acknowledged. Claims 25, 31, 32, 40, 41 have been amended. New claims 47-51 have been added. Claims 25, 27, 29, 31, 32, 35, 40, 41, 43 and 47-51 are pending in the application.

Election

2. Applicant's election Group I, claims 25, 27, 29, 31, 32, 35, 40, 41, 43 with respect to SEQID.NO: 2 without traverse 10/20/03 is acknowledged.

Priority

3. This application 371 is a national stage entry of 371 of PCT/EP00/01955 03/07/2000 which claims priority under 35, U.S.C. 119 (a)- (d)

UNITED KINGDOM 9905815.8 03/12/1999

UNITED KINGDOM 9909094.6 04/21/1999

UNITED KINGDOM 9909503.6 04/23/1999

UNITED KINGDOM 9909787.5 04/28/1999

UNITED KINGDOM 9910710.4 05/07/1999 is acknowledged. Claims 25, 27, 29, 31, 32, 35, 40, 41, 43 and 47-51 with respect SEQ.ID.NO: 2 comprising the 758 amino acid sequence is disclosed in the priority document UNITED KINGDOM 9905815.8 03/12/1999. Therefore priority is accorded as of 3/12/1999.

Drawings

4. No drawings have been filed in this application. However, the specification on pages 83-86 refers to sequences as shown in SEQ.ID.NO and further describes the sequences. However, it is not clear whether applicant refers these sequences under Sequence listing or

represented by figures. Applicant is advised to insert the Brief description of the drawings to the specification if these sequences are going to be represented by figures.

Information Disclosure Statement

5. The Information Disclosure Statement filed on 9/22/03 is signed and a copy of the same is attached with this office action.

Specification - Informalities

6. The specification on page 5 recites BASB043 polypeptide. However, there is no BASB043 polypeptide in the specification. The first page of the specification especially the title has missing letters. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 U.S. C. 112, first paragraph

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 25, 27, 29, 31, 32, 35, 40, 41, 43 and 47-51are rejected under 35 U.5.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is referred to the interim guidelines on written description published June 15, 1998 in the Federal Register at Volume 63, Number 114, pp 32639-32645 (also available at www.uspto.gov). This is a written description rejection.

The claims are drawn to an isolated polypeptide comprising a member selected from the group consisting of (a) the amino acid sequence matching SEQ.ID.NO: 2; (b) an immunogenic

fragment comprising at least 15 or 20 (the examiner is considering these as fragments) contiguous amino acids of SEQ.ID.NO: 2, where in the isolated polypeptide, when administered to a subject in a suitable composition which can include an adjuvant, or suitable carrier coupled to the polypeptide, induces an antibody or T-cell response that recognizes the polypeptide SEQ.ID.NO: 2.

The specification broadly describes as part of the invention, an isolated polypeptide comprising the amino acid sequence SEQ ID NO: 2, which are designated as a " BASB082 " polypeptide. The specification also teaches that this polypeptide has been obtained by recombinant cloning and contains 758 amino acids. The specification does not describe whether this polypeptide is able to recognize the sera obtained from infected individual. Moreover, the specification does not teach a fragment sequence of at least 15 or 20 contiguous amino acids of SEQ.ID.NO: 2. USPQ2d 1111 makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that (he or she] invented what is claimed." (See Vas-Cath at page 1116).

The actual biological function of the polypeptide as represented by SEQ ID NO: 2 is not set forth in this specification. An isolated polypeptide comprising the amino acid sequence, SEQ ID NO: 2 is uncharacterized by this specification and has not been shown to belong to any known family of proteins. The specification does not describe whether this polypeptide is able to recognize the sera obtained from infected individual. However, the actual structure of each fragment has not been described. There is no well-established correlation between structure and function of these fragments. It is noted that the claimed fragments do not exist as an independent invention. The specification fails to teach the structure or relevant identifying

characteristics of fragments of SEQ.ID.NO: 2, sufficient to allow one skilled in the art to determine that the inventor had possession of the invention as claimed. See Fiers v. Revel, 25 U5PQ2d 1601, 1606 (CAFC 1993) and Amgen Inc V Chugai Pharmaceutical Co Ltd., 18 U5PQ2d 1016. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 U5PQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class.

Thus, an isolated polypeptide comprising the amino acid sequence SEQ ID NO: 2 meets the written description provision of 35 U.S.C. 112, first paragraph.

12. Claims 25, 27, 29, 31, 32, 35, 40, 41, 43 and 47-51are rejected under 35 U.5.C. 112, first paragraph, because the specification, while being enabling for an isolated polypeptide comprising the amino acid sequence SEQ ID NO: 2, a fusion protein comprising the amino acid sequence SEQ.ID.NO: 2, and an immunogenic composition comprising the amino acid sequence SEQ.ID.NO: 2 and a pharmaceutically acceptable carrier does not reasonably provide enablement for a polypeptide comprising a fragment sequence of at least 15 or 20 (the examiner is considering these as fragments) contiguous amino acids of SEQ.ID.NO: 2, where in the isolated polypeptide, when administered to a subject in a suitable composition which can include an adjuvant, or suitable carrier coupled to the polypeptide, induces an antibody or T-cell response that recognizes the polypeptide SEQ.ID.NO: 2.

The claims are drawn to an isolated polypeptide comprising a member selected from the group consisting of (a) the amino acid sequence matching SEQ.ID.NO: 2; (b) an immunogenic fragment comprising at least 15 or 20 (the examiner is considering these as fragments) contiguous amino acids of SEQ.ID.NO: 2, where in the isolated polypeptide, when administered to a subject in a suitable composition which can include an adjuvant, or suitable carrier coupled

to the polypeptide, induces an antibody or T-cell response that recognizes the polypeptide SEQ.ID.NO: 2.

The instant claims are evaluated for scope of enablement based on the Wands analysis. Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731,8 USPQ2d 1400 (Fed.Circ.1988) as follows:

(1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The nature of the disclosed invention is an isolated polypeptide of SEQ ID NO: 2 from *Neisseria mengitidis* ATCC 13090 strain which is designated as a " BASB082" polypeptide in examples 1-5. The specification teaches that this polypeptide has been obtained by recombinant cloning and contains 758 amino acids. However, the specification is silent in disclosing whether this polypeptide recognizes antibodies that are obtained from Neisseria infected individuals. Further, the specification fails to indicate or teach any description of any such fragments that are able to bind to antisera raised against full-length polypeptide and provides no working examples demonstrating (i.e., guidance) enablement for any *fragments and* uses of the claimed polypeptide.

The state of the prior art indicates that protein chemistry is probably one of the most unpredictable areas of biotechnology and is highly complex. As taught by the prior art (Rudinger et al, in "PEPTIDE HORMONES", edited by Parsons, J.A., University Park Press, June 1976, page 6), the significance of any particular amino acid and sequences for different aspects of biological activity can not be predicted a priori and must be determined empirically on a case by case basis. The art specifically teaches that even a single amino acid change in a

protein leads to unpredictable changes in the biological activity of the protein. For example, replacement of a single lysine residue at position 118 of the acidic fibroblast growth factor by glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological-activity of the protein (Burgess et al., The Journal of Cell Biology, 111:2129-2138, 1990). In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine, or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biologic activity of the mitogen (Lazar et al., Molecular and Cellular Biology, 8(3): 1247-1252, 1988). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification, will often dramatically affect the biological activity of a protein. Proteins with replacement of a single amino acid residue may lead to both structural and functional changes in biological activity and immunological recognition. For example, Jobling et al. (Mol. Microbiol. 1991, 5(7): 1755-67) teaches a panel of single amino acid substitutions by oligonucleotide directed mutagenesis which products proteins that differ in native conformation, immunological recognition, binding and toxicity, thus exemplifying the importance of structural components to both biological function and immunological recognition.

In addition to the art-recognized unpredictability, the specification has not provided any guidance as to how an artisan would have dealt with the art recognized difficulties related to the unpredictability as raised above. The specification, however, provides no working examples demonstrating enablement for making and using the claimed fragments. Thus, making and using fragments of a polypeptide must be considered highly unpredictable, requiring a specific demonstration. Absent such demonstration, the skilled artisan would be forced into undue experimentation to make and use the invention commensurate in scope with these claims.

Status of Claims

13. No claims are allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padma Baskar whose telephone number is (703) 308-8886. The examiner can normally be reached on Monday through Friday from 6:30 AM to 4 PM EST

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned is (703) 872.9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Padma Baskar Ph.D.

1/11/04

LRS

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